REMARKS

Claims 2-14 are now pending, claim 1 having been cancelled and claims 5, 9, 10, and 12 having been replaced by the above amendments. The amendments to claims 5, 9, 10, and 12 are made to correct typographical errors or omissions and to bring recitation of Markush groups in compliance with USPTO practice. Accordingly, these amendments do not narrow the scope of any pending claim as originally filed.

Reconsideration of the pending claims is requested in view of the following remarks.

The Examiner objects to the specification for failing to provide an abstract on a separate sheet. Applicant has amended the specification to insert a new page 12 reciting the abstract, thereby overcoming the objection.

The Examiner has rejected claim 1 as indefinite under 35 U.S.C. § 112, second paragraph, and as ineligible for patenting under 35 U.S.C. § 101. Applicant has canceled claim 1, rendering these rejections moot.

I

Claims 1-14 are rejected under 35 U.S.C. § 103(a) as obvious over Schluep et al., Med et Hyg 55:33-35, 1997. Claim 1 has been cancelled. This rejection is traversed.

According to the Examiner, it is unclear from the English abstract of this reference whether treatments for amyotrophic lateral sclerosis (ALS), including administration of riluzole, is applied by Schluep to multiple sclerosis (MS). Applicant provides herewith a copy of the full Schluep reference in French as well as an English translation of Schluep ("Translation"). It is quite clear that Schluep's description of riluzole as a treatment for ALS cannot be extended to MS, and therefore this rejection should be withdrawn.

Schluep briefly summarizes the knowledge, or lack thereof, of the etiology of ALS and MS at the paragraph bridging pages 1 and 2 of the Translation. Schluep notes that, while MS is of autoimmune origin and leads to loss of myelin and oligodendrocytes, ALS is characterized by neurodegeneration of unknown cause and loss of *motor neurons*.

Schluep then speculates that etiology of ALS may involve *glutamate-associated excitotoxicity* among other causes. Thus, ALS and MS differ not only in the type of cell in which disease is manifested, but apparently also in the root cause of the disease.

At page 2-3 of the Translation, Schluep reviews the use of riluzole, a glutamate inhibitor, as a drug for treatment of ALS. Given the etiological background provided by Schluep and discussed above, it is clear that Schluep does not describe nor suggest the use of riluzole for treatment of MS. Schluep provides no link between glutamate excitotoxicity and the etiology of MS, no link between inhibition of glutamate and MS therapy, and therefore no link between riluzole and MS treatment. These are rather substantial deficiencies in the Examiner's basis for this obviousness rejection, and accordingly, the rejection should be withdrawn.

II

Claims 1-14 are rejected under 35 U.S.C. § 103(a) as obvious over Arnold et al. (WO 98/41882). Claim 1 has been cancelled. The rejection is traversed.

According to the Examiner, Arnold describes drugs such as riluzole to "treat neurodegenerative disease for which N-acetylaspartate decline has been observed, as in multiple sclerosis." Page 3, last paragraph, of the Office Action. The Examiner specifically cites page 6, lines 8-13, of Arnold for this conclusion. Applicant respectfully disagrees with the conclusion and the basis for it.

Though subtle, the distinction between the Examiner's basis and what Arnold actually states is critical. Yes, Arnold does disclose that riluzole treats ALS and that ALS is characterized by abnormally low NAA. See page 5, lines 1-20, of Arnold. But no, nowhere does Arnold describe or suggest that riluzole would be effective against MS, even if a specific manifestation of MS may also be characterized by low NAA. Rather, a careful reading of the passage in Arnold cited by the Examiner indicates that Arnold states only that NAA can be used as a surrogate marker for testing drugs in other conditions such as acute exacerbations of MS. Page 6, lines 7-24, of Arnold. Arnold

never says which drugs should be tested in this form of MS, much less which drugs would be effective in treating MS.

At best, Arnold links acute episodes of MS with ALS by a common surrogate marker, NAA, but a common surrogate marker does not lead to a common etiology or therapeutic strategy. By analogy, the Examiner's reasoning would lead to the following conclusion: A driver in a pick-up truck speeds through a stop sign and crashes into another vehicle. The driver was speeding because he was trying to take his unconscious wife and passenger to the hospital. It is determined that making ambulances more readily available was a solution that could have prevented the accident. A bank robber robs a bank and escapes in a pick-up truck. The robber speeds through a stop sign and crashes into another vehicle. Does the city conclude that bank robberies can be prevented by making ambulances more readily available? Of course not, because there is no link between ambulances and bank robberies, even though the surrogate marker, the crash from running the stop sign, was common to both events. Likewise, Arnold does not provide a link between the etiology of MS with the etiology of ALS, and the skilled artisan cannot suspect that riluzole would be effective in treating MS.

Indeed, the skilled artisan at the time of filing of the instant application would not have thought of testing riluzole for efficacy against MS, much less have thought that riluzole would be efficacious against MS. As discussed in regard to Schluep above and confirmed in Arnold, ALS is a disease of neurons, not accessory cells as Schluep says is the case in MS. Arnold recognizes, therefore, that riluzole is one of a variety of drugs that can treat neurons. Page 6, lines 1-6, of Arnold. Arnold does not contemplate riluzole as a candidate drug for MS. In this regard, even Arnold's cursory mention of "acute exacerbations of multiple sclerosis" at page 6, lines 12-13 must be treated as mere speculation, since Arnold elsewhere tells us that NAA is exclusively found in neurons and neuronal processes in the normal mature brain. Pages 1-2, bridging sentence, of Arnold.

Even if the Examiner were to conclude that Arnold describes riluzole as an agent that could be tested for treating MS, it is clear, by Arnold's own teachings, that this is merely an "obvious to try" disclosure without the requisite "expectation of success." Applicant has already indicated the reasons why, at the time of Applicant's disclosure, the skilled artisan would discount riluzole as being relevant to treatment of MS.

In light of the foregoing, it is respectfully maintained that each of pending claims 2-14 are patentable and in a condition for allowance.

A Petition for Three-Month Extension of Time is filed herewith.

Respectfully submitted,

John T. Li

John T. Li
Reg. No. 44,210
BIOGEN, INC.
14 Cambridge Center
Cambridge, MA 02142
(617) 914-4704

Date: 2-6-03

doc# 12468

Version Showing Mark-Ups

Deleted text is shown using ~~strikethrough~~ and added text is shown using underlining.

In the Claims

5. The method of claim 4 wherein said additional agent is selected from the group consisting of interferon beta -1a, interferon beta -1b, ~~or~~and copaxone.

9. The method of claim 8 wherein said pharmaceutical composition further comprises a therapeutically or prophylactically effective amount of an additional agent selected from the group consisting of ~~intereferon~~interferon beta -1b, interferon beta -1a, ~~or~~and copaxone.

10. A method for the treatment of a patient suffering from MS comprising the steps of administering to said patient:

a. a therapeutically effective amount of a pharmaceutical composition comprising ~~riluzole~~riluzole; and

b. a therapeutically effective amount of a pharmaceutical composition selected from the group consisting of interferon beta -1b, interferon beta -1a, ~~or~~and copaxone.

12. The method of claim 11 further comprising the administration of a therapeutically effective amount of interferon beta -1b, copaxone ~~or~~and interferon beta-1a.

Abstract of the Disclosure

A1

The invention relates to treatment of multiple sclerosis in a subject by administering 6-(trifluoromethoxy)-benzothiazolamine, also known as riluzole, to the subject.